Remarks

Claims 46-50, 55, and 57-60 are pending in the subject application and currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Claims 46-50, 55 and 57-60 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Tang *et al.* (WO 02/074961). As noted previously, Tang *et al.* states, at page 7, lines 3-7:

> The polypeptides of the present invention and the polynucleotides encoding them are also useful **for the same functions known to one of skill in the art as the polypeptides and polynucleotides to which they have homology** (set forth in Table 2); **for which they have a signature region** (as set forth in Table 3); or **for which they have homology to a gene family** (as set forth in Table 4). (emphasis added)

Applicants also noted that the polypeptide corresponding to SEQ ID NO: 913 is not associated with a polypeptide useful for the treatment of liver or lung fibrosis. Thus, it cannot be said that the reference teaches or suggests its use in such a treatment protocol. Particularly, Table 2 indicates that the polypeptide has homology to the human SEC protein of the *sec* oncogene or a human hematopoietic/immune antigen (see Table 2, page 177). The polypeptide is not listed in Tables 3 or 4; thus, the polypeptide was not recognized as having homology to a signature region or homology to a gene family at the time the cited reference was filed. Thus, at best, one skilled in the art, in view of the teachings of the reference, would have used the polypeptide associated with SEQ ID NO: 913 in methods of detecting cancers or, possibly, for detecting elements of the human hematopoietic/immune systems. Indeed, the description of the reference would indicate that a polypeptide with similarities to an oncogene of a human hematopoietic/immune antigen would be used in assays such as those discussed at sections 3.10.3-3.10.5 (see pages 47-53) or section 3.10.11 (pages 64-66). The teachings of the reference would not have indicated that the claimed polypeptide should have been used for the treatment of liver or lung fibrosis.

In maintaining the rejection of record, the Office Action argues:

> Applicant's arguments have been fully considered but are not found persuasive. Applicant's arguments that the polypeptide has homology to the human SEC protein of the sec oncogene or a human hematopoietic/immune antigen and that at best, one skilled in the art, in view of the teachings of the reference, would have used the polypeptide associated with SEQ ID NO:913 in methods of detecting cancers or possibly for detecting elements of the human hematopoietic/immune systems is not found persuasive because relevant literature reports examples of

polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities. For example, Tischer *et al.* (U.S. Patent 5,194,596) establishes that VEGF (a member of the platelet-derived growth factor (PDGF) family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). Vukicevic *et al.* (PNAS USA 93:9021-9026, 1996) disclose that OP-1, a member of the TGF-β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF-β family members BMP-2 and TGF-β1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Even if the protein of Tang *et al.* has homology to a human hematopoietic/immune antigen or the human SEC protein does not mean that the protein must only be employed in methods of detecting elements of the human hematopoietic/immune system or methods of detecting cancer. Tang *et al.* clearly teach a 163 amino acid polypeptide that is 100% identical to instant SEQ ID NO:2, which is 163 amino acids. Tang *et al.* clearly teach that the composition of the present invention is useful for treatment of lung or liver fibrosis (page 55, lines 24-26).

Applicants maintain that this rationale for maintaining the rejection of record is clearly improper as it requires one skilled in the art to ignore the express teachings of Tang *et al.* (the disclosed polypeptides and polynucleotides are "useful for the same functions known to one of skill in the art as the polypeptides and polynucleotides to which they have homology (set forth in Table 2); for which they have a signature region (as set forth in Table 3); or for which they have homology to a gene family (as set forth in Table 4)"). Furthermore, the Office Action argues that one skilled in the art would have had to proceed along this course of action on the off chance that the polypeptide of SEQ ID NO: 913 would have had a biological activity completely unrelated to that disclosed within the reference.

Applicants further submit that the rejection of record is improper as it requires one skilled in the art to pick and choose various disclosures within Tang *et al.* that are not directly related to one another and then proceed in a manner completely contrary with respect to how the reference teaches one to use the disclosed polypeptides in order to arrive at the claimed invention. As stated in the Office Action, Applicants' arguments were "not found persuasive because relevant literature reports examples of polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities".

As stated in *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1083, 89 U.S.P.Q.2d 1370 (Fed. Cir.2008):

> In order to anticipate, the reference "must clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without ***any*** need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference." *In re Arkley,* 59 C.C.P.A. 804, 455 F.2d 586, 587 (1972). (emphasis in original).

In this case, Tang *et al.,* describes 526 different polynucleotides (SEQ ID NOs: 1-526) and the corresponding polypeptides (SEQ ID NOs: 527-1052), among which SEQ ID NO: 913 is 100% identical to SEQ ID NO: 2. Tang *et al.* disclose that a composition may also be useful for treatment of lung or liver fibrosis (page 55, lines 24-26). However, Applicants note that:

- SEQ ID NO: 913 is one of 1052 disclosed sequences;
- "Lung or liver fibrosis" are two disorders listed among hundreds of very disparate diseases or disorders that may be treated by a composition according to Tang *et al.* and SEQ ID NO: 913 is not disclosed as having sequence homology to proteins that might be useful in such a context; and
- The wording "composition", according to Tang *et al.,* does not mean only "polypeptide" but includes among others, polypeptides, polynucleotides encoding such polypeptides, degenerate variants, antibodies, hybridomas producing such antibodies, binding partners for the polypeptides or modulators (page 2, lines 1-6 and page 76, lines 6-7).

Thus, one skilled in the art would have had to select:

1) A sequence having no homology to proteins (or polynucleotides encoding proteins) associated with liver fibrosis from the 1052 disclosed sequences for use in a method of treatment;
2) A disease from the many hundreds of various diseases/disorders listed in the as-filed description (lung and liver fibrosis); and
3) The type of composition useful for treating such disease, *i.e.*, polypeptides, polynucleotides encoding such polypeptides, degenerate variants, antibodies,

hybridomas producing such antibodies, binding partners for the polypeptides or modulators or the polypeptides or polynucleotides.

Nothing in Tang *et al.* directs the skilled artisan to the selection of "SEQ ID NO. 913" from list 1, "liver or lung disorder" from list 2 and "polypeptide" from list 3. Furthermore, not only would one skilled in the art have had to ignore the express teachings of Tang *et al.* (that the polypeptides and polynucleotides disclosed in Tang *et al.* are useful for the same functions known to one of skill in the art as the polypeptides and polynucleotides to which they have homology (set forth in Table 2); for which they have a signature region (as set forth in Table 3); or for which they have homology to a gene family (as set forth in Table 4); see page 7, lines 3-7), but that person would also have had to select specific elements from 3 different and unrelated "lists" disclosed in Tang *et al.* in order to arrive to the presently claimed invention. Accordingly, it is respectfully submitted that Tang *et al.* fails to anticipate the claimed invention as it does not teach the specific arrangement of the present invention, *i.e.*, a method for treating a fibrotic disease comprising administering a composition comprising a polypeptide comprising SEQ ID NO. 2, wherein said fibrotic disease is lung fibrosis or liver fibrosis and one skilled in the art is forced to pick, choose, and combine various disclosures not directly related to each other in order to arrive at the claimed invention.

Applicants further note that the Office Action argues that the previously submitted arguments are not persuasive. To support this position, the Office Action argues that "[SEQ ID No. 913] of Tang *et al.* has homology to a human hematopoietic/immune antigen or to the human SEC protein does not mean that the protein must only be employed in methods of detecting elements of the human hematopoietic/immune system or methods of detecting cancer" and it is argued that the "literature reports examples of polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities". Notably, Tischer *et al.* and Vukicevic *et al.* are cited in support of this position. However, and contrary to Examiner's assertion, these references do not teach that individual members of a superfamily of proteins have opposite activities. These references underscore the fact that members of the same family may have same activity but on different cell types or on different tissues. Tischer *et al.* describe that PDGF is mitogenic for vascular smooth muscle and VEGF is mitogenic for vascular endothelial cells. Vukicevic *et al.* describe that

OP1/BMP7 protein, belonging to the TGFβ superfamily, mediates an early inductive signal for metanephric differentiation during the development of vertebrate kidney. Although this document teaches that BMP-2, a closely related member of the TGFβ superfamily and TGFβ1 had no effect on metanephric differentiation under identical conditions, it is known that BMP-2 is involved in cardiac cell differentiation and that TGFβ1 is required for endothelial differentiation. Thus, it is respectfully submitted that reliance on Tischer *et al.* and Vukicevic *et al.* fail to remedy the defects noted in the rejection and cannot support a finding that the claimed invention is anticipated by Tang *et al.* Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e) is respectfully requested.

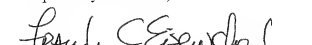
Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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